

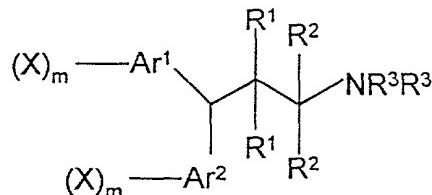
Claims

1. A method of treating a patient for depression comprising the step of administering to said patient an effective amount of a compound having a NMDA IC₅₀ of about 50 nM to about 1 μ M as measured in the NMDA assay and a serotonin reuptake IC₅₀ of less than or equal to about 100 nm as measured in the serotonin reuptake inhibition assay.

2. The method of claim 1, wherein said compound has an NMDA receptor IC₅₀ of 50 nM to 1 μ M and a SSRI IC₅₀ less than 100 nM.

3. A method of treating a patient for depression comprising the step of administering to said patient an effect amount of a compound having the chemical structure:

15



wherein each X is independently selected from the group consisting of -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃, -O-alkyl, and -O-acyl;

Ar¹ and Ar² are each independently selected from the group consisting of phenyl, naphthyl, thiofuranyl, tetrahydronaphthyl, furanyl, tetrahydrofuranyl, pyridyl, quinolinyl, isoquinolinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, cyclohexyl, cycloheptyl, and cyclopentyl;

each R¹ is independently selected from the group consisting of -H, alkyl, hydroxyalkyl, -OH, -O-alkyl, and -O-acyl;

each R² is independently selected from the group consisting of -H, alkyl, and hydroxyalkyl, or both R²'s together are imino;

each R^3 is independently selected from the group consisting of -H, alkyl, 2-hydroxyethyl, and alkylphenyl; and each m is independently an integer from 0 to 5; provided that if both R_3 's are -CH₃, then both X_m 's are not 5 3-F, 4-F, 3-CF₃, 4-Cl, and if both R_3 's are -CH₃, and one X_m is 4-F then the other X_m is not 4-Cl; further provided that if one R_3 is -H and the other R_3 is -CH₃ then both X_m 's are not 4-Cl, and if one R_3 is -H and the other R_3 is -CH₃ then at least one m is 1; or a pharmaceutically acceptable salt thereof.

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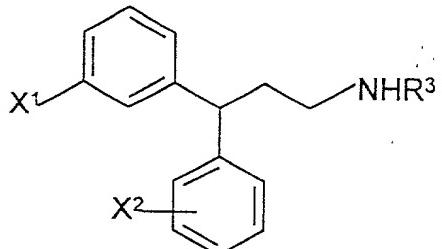
4. The method of claim 3 wherein for said compound each X is independently either -F, -Cl, -OCF₃ or -CF₃;

each R^1 is -H;

each R^2 is -H;

15 one R^3 is -H, and the other R^3 is either -H or -CH; and each m is 1.

5. The method of claim 3 wherein said compound has the chemical structure:



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wherein X¹ is either -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃, -O-alkyl, or -O-acyl;

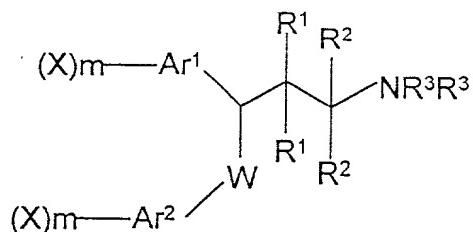
25 X² is either -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃, -O-alkyl, or -O-acyl; and

R³ is either -H or -CH₃;

or a pharmaceutically acceptable salt thereof.

6. The method of claim 5, wherein X¹ is -F, -Cl, -OCF₃, or -CF₃; and X² is either 2-OCH₃, 2-CH₃, 3-F, 3-CF₃, or 4-CF₃.

7. A method of treating a patient for depression comprising the step of administering to said patient an effect amount of a compound having the chemical structure:



5

wherein each X is independently selected from the group consisting of -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃, -O-alkyl, and -O-acyl;

Ar¹ and Ar² are each independently selected from the group consisting of phenyl, naphthyl, thiofuranyl, tetrahydronaphthyl, furanyl, tetrahydrofuranyl, pyridyl, quinolinyl, isoquinolinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl cyclohexyl, cycloheptyl, and cyclopentyl;

each R¹ is independently selected from the group consisting of -H, alkyl, hydroxyalkyl, -OH, -O-alkyl, and -O-acyl;

each R² is independently selected from the group consisting of -H, alkyl, and hydroxyalkyl, or both R²'s together are imino;

each R³ is independently selected from the group consisting of -H, alkyl, 2-hydroxyethyl, and alkylphenyl; and

20 m is 0 to 5;

or a pharmaceutically acceptable salt thereof.

8. The method of claim 7, wherein for said compound each X is independently either -F, -Cl, -OCF₃, or -CF₃;

25 Ar¹ and Ar² are each independently phenyl or naphthyl;

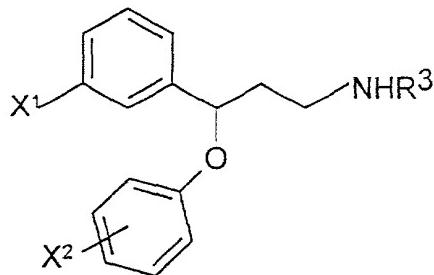
each R¹ is -H;

each R² is -H;

one R³ is -H, and the other R³ is either -H or -CH₃;

each m is 0 or 1.

9. The method of claim 7, wherein said compound has the chemical structure:



5 wherein X^1 is either -Br, -Cl, -F, -I, -CF₃, alkyl, -OH,
-OCF₃, -O-alkyl, or -O-acyl;

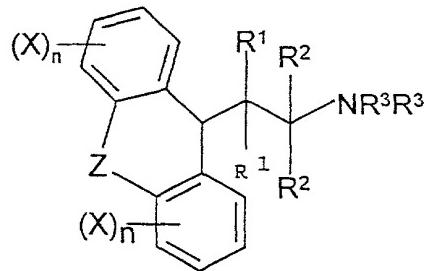
X^2 is either -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃,
-O-alkyl, or -O-acyl; and

 R³ is either -H or -CH₃;

10 or a pharmaceutically acceptable salt thereof.

10. The method of claim 9 wherein X^1 is either -F, -Cl,
-OCF₃ or -CF₃; and X^2 is either 2-OCH₃, 2-CH₃, 3-F, 3-CF₃, or 4-CF₃.

15 11. A method of treating a patient for depression comprising the step of administering to said patient an effect amount of a compound having the chemical structure:



20 wherein each X is independently selected from the group consisting of -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃,
-O-alkyl, and -O-acyl;

each R¹ is independently selected from the group consisting of -H, alkyl, hydroxyalkyl, -OH, -O-alkyl, and -O-acyl;

each R² is independently selected from the group consisting of -H, alkyl, and hydroxyalkyl, or both R²'s together are imino;

5 each R³ is independently selected from the group consisting of -H, alkyl, 2-hydroxyethyl, and alkylphenyl;

Z is either -CH₂CH₂-, -CH₂CH(CH₃)-, -CH=CH-, -O-CH₂-, -S-CH₂-, -CH₂-, -O-, or -S-; and

10 each n is independently 1 to 4; or a pharmaceutically acceptable salt thereof.

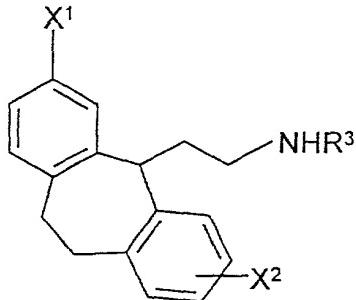
12. The compound of claim 11, wherein each X is independently either -F, -Cl, -OCF₃ or -CF₃;

each R¹ is -H;

each R² is -H;

15 one R³ is -H, and the other R³ is either -H or -CH; and each n is 1.

13. The method of claim 11, wherein said compound has the chemical structure:



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wherein X¹ is either -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃, -O-alkyl, or -O-acyl;

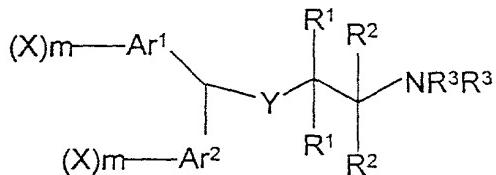
X² is either -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃, -O-alkyl, or -O-acyl; and

25 R³ is either -H or -CH₃;

or a pharmaceutically acceptable salt thereof.

14. The method of claim 13 wherein X^1 is -F, -Cl, -OCF₃, or -CF₃; and X^2 is either either -F, -Cl, -OCH₃, -CH₃, -OCF₃ or -CF₃.

5 15. A method of treating a patient for depression comprising the step of administering to said patient an effect amount of a compound having the chemical structure:



10 wherein each X is independently selected from the group consisting of -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃, -O-alkyl, and -O-acyl; preferably, each X is independently either -F, -Cl, -OCF₃ or -CF₃;

15 Ar¹ and Ar² are each independently selected from the group consisting of phenyl, naphthyl, thiofuranyl, tetrahydronaphthyl, furanyl, tetrahydrofuranyl, pyridyl, quinolinyl, isoquinolinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, cyclohexyl, cycloheptyl, and cyclopentyl; preferably Ar¹ and Ar² are independently naphthyl or phenyl; more preferably at least one of
20 Ar¹ and Ar² is phenyl; and more preferably, both Ar¹ and Ar² are phenyl;

Y is either -CH₂-, -O-, or -S-;

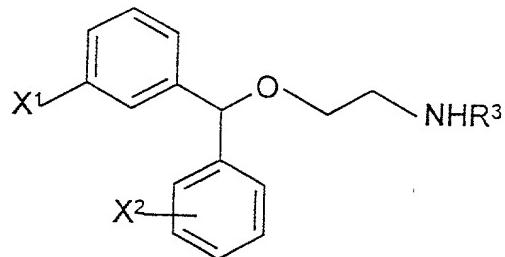
each R¹ is independently selected from the group consisting of -H, alkyl, hydroxyalkyl, -OH, -O-alkyl, and -O-acyl; 25 preferably, each R¹ is -H;

each R² is independently selected from the group consisting of -H, alkyl, and hydroxyalkyl, or both R²'s together are imino; preferably each R² is -H;

each R³ is independently selected from the group consisting 30 of -H, alkyl, 2-hydroxyethyl, and alkylphenyl; preferably, each R³ is independently either -H or -CH₃; more preferably one R³ is -H, and the other R³ is either -H or -CH₃; and

each m is independently an integer from 0 to 5; and preferably, each m is independently 0 or 1.

- 5 16. The method of claim 15, wherein said compound has the chemical structure; Structure VIII



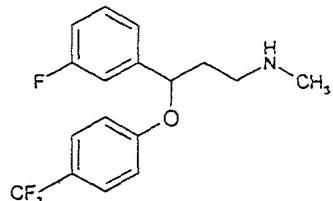
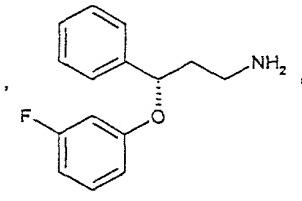
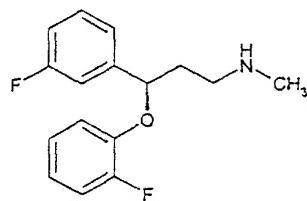
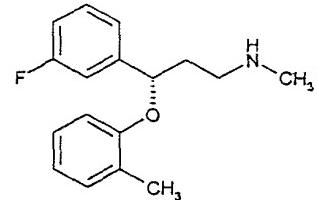
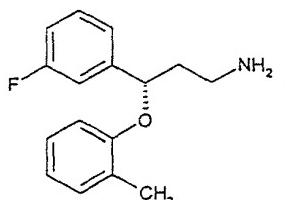
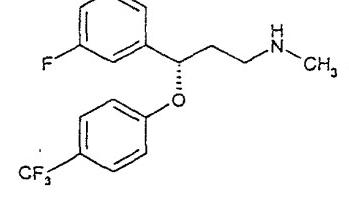
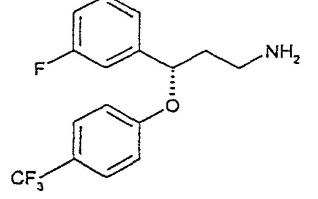
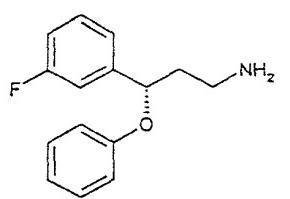
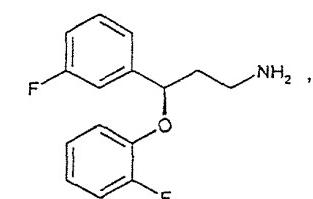
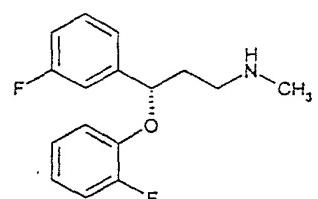
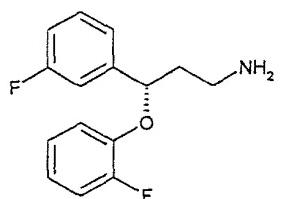
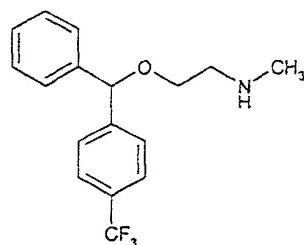
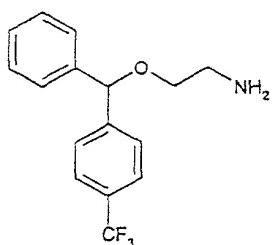
wherein X¹ is independently selected from the group consisting of -H, -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃, -O-alkyl, or -O-acyl; preferably, X¹ is either -F, -Cl, -OCF₃ and -CF₃;

10 X² is either -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃, -O-alkyl, or -O-acyl; preferably, X² is independently either -F, -Cl, -OCH₃, -CH₃, -OCF₃ or -CF₃; more preferably, X² is either 2-

15 OCH₃, 2-CH₃, 3-F, 3-CF₃, or 4-CF₃; and R³ is either -H or CH₃;

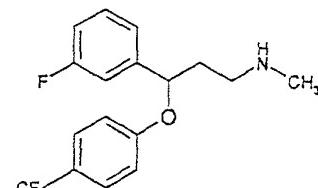
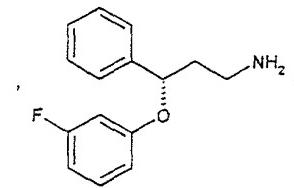
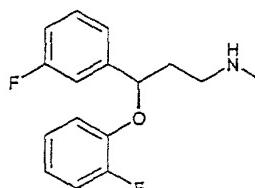
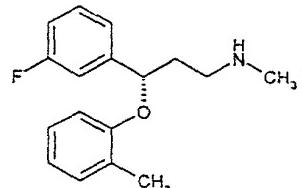
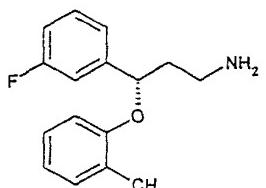
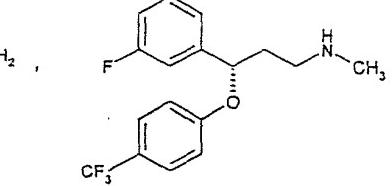
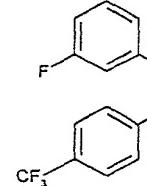
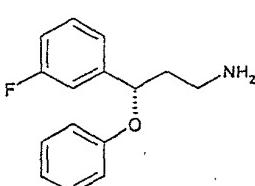
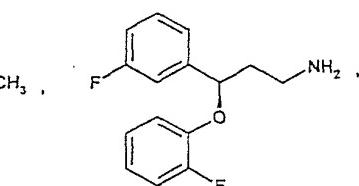
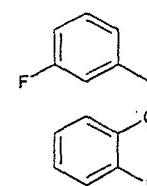
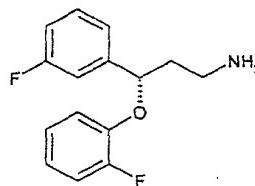
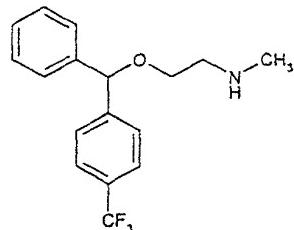
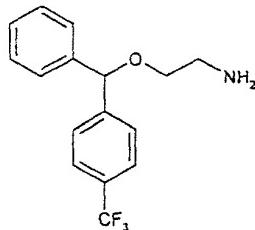
or a pharmaceutically acceptable salt thereof.

17. A compound having the chemical structure;



or a pharmaceutically acceptable salt thereof.

18. A method of treating a patient for depression comprising the step of administering to said patient an effect amount of a compound having the chemical structure:



5 or a pharmaceutically acceptable salt thereof.